



1

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<110> PAKOLA, STEVE  
DE SMET, MARK

<120> PHARMACOLOGICAL VITREOLYSIS

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<141> 2003-12-05

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<151> 2002-12-06

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<170> PatentIn Ver. 3.2

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10

15

cct gga agg gtt gtg ggg ggg tgt gtg gcc cac cca cat tcc tgg ccc	96
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tgg caa gtc agt ctt aga aca agg ttt gga atg cac ttc tgt gga ggc	144
Trp Gln Val Ser Leu Arg Thr Arg Phe Gly Met His Phe Cys Gly Gly	
35 40 45	
acc ttg ata tcc cca gag tgg gtg ttg act gct gcc cac tgc ttg gag	192
Thr Leu Ile Ser Pro Glu Trp Val Leu Thr Ala Ala His Cys Leu Glu	
50 55 60	
aag tcc cca agg cct tca tcc tac aag gtc atc ctg ggt gca cac caa	240
Lys Ser Pro Arg Pro Ser Ser Tyr Lys Val Ile Leu Gly Ala His Gln	
65 70 75 80	
gaa gtg aat ctc gaa ccg cat gtt cag gaa ata gaa gtg tct agg ctg	288
Glu Val Asn Leu Glu Pro His Val Gln Glu Ile Glu Val Ser Arg Leu	
85 90 95	
ttc ttg gag ccc aca cga aaa gat att gcc ttg cta aag cta agc agt	336
Phe Leu Glu Pro Thr Arg Lys Asp Ile Ala Leu Leu Lys Leu Ser Ser	
100 105 110	
cct gcc gtc atc act gac aaa gta atc cca gct tgt ctg cca tcc cca	384
Pro Ala Val Ile Thr Asp Lys Val Ile Pro Ala Cys Leu Pro Ser Pro	
115 120 125	
aat tat gtg gtc gct gac cgg acc gaa tgt ttc atc act ggc tgg gga	432
Asn Tyr Val Val Ala Asp Arg Thr Glu Cys Phe Ile Thr Gly Trp Gly	
130 135 140	
gaa acc caa ggt act ttt gga gct ggc ctt ctc aag gaa gcc cag ctc	480
Glu Thr Gln Gly Thr Phe Gly Ala Gly Leu Leu Lys Glu Ala Gln Leu	
145 150 155 160	
cct gtg att gag aat aaa gtg tgc aat cgc tat gag ttt ctg aat gga	528
Pro Val Ile Glu Asn Lys Val Cys Asn Arg Tyr Glu Phe Leu Asn Gly	
165 170 175	
aga gtc caa tcc acc gaa ctc tgt gct ggg cat ttg gcc gga ggc act	576
Arg Val Gln Ser Thr Glu Leu Cys Ala Gly His Leu Ala Gly Gly Thr	
180 185 190	
gac agt tgc cag ggt gac agt gga ggt cct ctg gtt tgc ttc gag aag	624
Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Phe Glu Lys	
195 200 205	
gac aaa tac att tta caa gga gtc act tct tgg ggt ctt ggc tgt gca	672
Asp Lys Tyr Ile Leu Gln Gly Val Thr Ser Trp Gly Leu Gly Cys Ala	
210 215 220	
cgc ccc aat aag cct ggt gtc tat gtt cgt gtt tca agg ttt gtt act	720
Arg Pro Asn Lys Pro Gly Val Tyr Val Arg Val Ser Arg Phe Val Thr	
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 35 40 45  
 Thr Leu Ile Ser Pro Glu Trp Val Leu Thr Ala Ala His Cys Leu Glu  
 50 55 60  
 Lys Ser Pro Arg Pro Ser Ser Tyr Lys Val Ile Leu Gly Ala His Gln  
 65 70 75 80  
 Glu Val Asn Leu Glu Pro His Val Gln Glu Ile Glu Val Ser Arg Leu  
 85 90 95  
 Phe Leu Glu Pro Thr Arg Lys Asp Ile Ala Leu Leu Lys Leu Ser Ser  
 100 105 110  
 Pro Ala Val Ile Thr Asp Lys Val Ile Pro Ala Cys Leu Pro Ser Pro  
 115 120 125  
 Asn Tyr Val Val Ala Asp Arg Thr Glu Cys Phe Ile Thr Gly Trp Gly  
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 Glu Thr Gln Gly Thr Phe Gly Ala Gly Leu Leu Lys Glu Ala Gln Leu  
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 165 170 175  
 Arg Val Gln Ser Thr Glu Leu Cys Ala Gly His Leu Ala Gly Gly Thr  
 180 185 190  
 Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Phe Glu Lys  
 195 200 205  
 Asp Lys Tyr Ile Leu Gln Gly Val Thr Ser Trp Gly Leu Gly Cys Ala  
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 Primer

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 <222> (1)..(1044)

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 Glu Asp Cys Met Phe Gly Asn Gly Lys Gly Tyr Arg Gly Lys Arg Ala  
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 acc act gtt act ggg acg cca tgc cag gac tgg gct gcc cag gag ccc 144  
 Thr Thr Val Thr Gly Thr Pro Cys Gln Asp Trp Ala Ala Gln Glu Pro  
 35 40 45  
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 His Arg His Ser Ile Phe Thr Pro Glu Thr Asn Pro Arg Ala Gly Leu  
 50 55 60  
 gaa aaa aat tac tgc cgt aac cct gat ggt gat gta ggt ggt ccc tgg 240  
 Glu Lys Asn Tyr Cys Arg Asn Pro Asp Gly Asp Val Gly Gly Pro Trp  
 65 70 75 80

tgc tac acg aca aat cca aga aaa ctt tac gac tac tgt gat gtc cct	288
Cys Tyr Thr Thr Asn Pro Arg Lys Leu Tyr Asp Tyr Cys Asp Val Pro	
85 90 95	
cag tgt gcg gcc cct tca ttt gat tgt ggg aag cct caa gtg gag ccg	336
Gln Cys Ala Ala Pro Ser Phe Asp Cys Gly Lys Pro Gln Val Glu Pro	
100 105 110	
aag aaa tgt cct gga agg gtt gtg ggg ggg tgt gtg gcc cac cca cat	384
Lys Lys Cys Pro Gly Arg Val Val Gly Gly Cys Val Ala His Pro His	
115 120 125	
tcc tgg ccc tgg caa gtc agt ctt aga aca agg ttt gga atg cac ttc	432
Ser Trp Pro Trp Gln Val Ser Leu Arg Thr Arg Phe Gly Met His Phe	
130 135 140	
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Cys Gly Gly Thr Leu Ile Ser Pro Glu Trp Val Leu Thr Ala Ala His	
145 150 155 160	
tgc ttg gag aag tcc cca agg cct tca tcc tac aag gtc atc ctg ggt	528
Cys Leu Glu Lys Ser Pro Arg Pro Ser Ser Tyr Lys Val Ile Leu Gly	
165 170 175	
gca cac caa gaa gtg aat ctc gaa ccg cat gtt cag gaa ata gaa gtg	576
Ala His Gln Glu Val Asn Leu Glu Pro His Val Gln Glu Ile Glu Val	
180 185 190	
tct agg ctg ttc ttg gag ccc aca cga aaa gat att gcc ttg cta aag	624
Ser Arg Leu Phe Leu Glu Pro Thr Arg Lys Asp Ile Ala Leu Leu Lys	
195 200 205	
cta agc agt cct gcc gtc atc act gac aaa gta atc cca gct tgt ctg	672
Leu Ser Ser Pro Ala Val Ile Thr Asp Lys Val Ile Pro Ala Cys Leu	
210 215 220	
cca tcc cca aat tat gtg gtc gct gac cgg acc gaa tgt ttc atc act	720
Pro Ser Pro Asn Tyr Val Val Ala Asp Arg Thr Glu Cys Phe Ile Thr	
225 230 235 240	
ggc tgg gga gaa acc caa ggt act ttt gga gct ggc ctt ctc aag gaa	768
Gly Trp Gly Glu Thr Gln Gly Thr Phe Gly Ala Gly Leu Leu Lys Glu	
245 250 255	
gcc cag ctc cct gtg att gag aat aaa gtg tgc aat cgc tat gag ttt	816
Ala Gln Leu Pro Val Ile Glu Asn Lys Val Cys Asn Arg Tyr Glu Phe	
260 265 270	
ctg aat gga aga gtc caa tcc acc gaa ctc tgt gct ggg cat ttg gcc	864
Leu Asn Gly Arg Val Gln Ser Thr Glu Leu Cys Ala Gly His Leu Ala	
275 280 285	
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290 295 300	

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35 40 45

His Arg His Ser Ile Phe Thr Pro Glu Thr Asn Pro Arg Ala Gly Leu
50 55 60

Glu Lys Asn Tyr Cys Arg Asn Pro Asp Gly Asp Val Gly Gly Pro Trp
65 70 75 80

Cys Tyr Thr Thr Asn Pro Arg Lys Leu Tyr Asp Tyr Cys Asp Val Pro
85 90 95

Gln Cys Ala Ala Pro Ser Phe Asp Cys Gly Lys Pro Gln Val Glu Pro
100 105 110

Lys Lys Cys Pro Gly Arg Val Val Gly Gly Cys Val Ala His Pro His
115 120 125

Ser Trp Pro Trp Gln Val Ser Leu Arg Thr Arg Phe Gly Met His Phe
130 135 140

Cys Gly Gly Thr Leu Ile Ser Pro Glu Trp Val Leu Thr Ala Ala His
145 150 155 160

Cys Leu Glu Lys Ser Pro Arg Pro Ser Ser Tyr Lys Val Ile Leu Gly
165 170 175

Ala His Gln Glu Val Asn Leu Glu Pro His Val Gln Glu Ile Glu Val
180 185 190

Ser Arg Leu Phe Leu Glu Pro Thr Arg Lys Asp Ile Ala Leu Leu Lys
195 200 205

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Leu Ser Ser Pro Ala Val Ile Thr Asp Lys Val Ile Pro Ala Cys Leu  
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 Pro Ser Pro Asn Tyr Val Val Ala Asp Arg Thr Glu Cys Phe Ile Thr  
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 275 280 285  
 Gly Gly Thr Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys  
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 Lys Cys Glu Glu Asp Glu Glu Phe Thr Cys Arg Ala Phe Gln Tyr His  
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 agt aaa gag caa caa tgt gtg ata atg gct gaa aac agg aag tcc tcc 192  
 Ser Lys Glu Gln Gln Cys Val Ile Met Ala Glu Asn Arg Lys Ser Ser  
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 ata atc att agg atg aga gat gta gtt tta ttt gaa aag aaa gtg tat 240  
 Ile Ile Ile Arg Met Arg Asp Val Val Leu Phe Glu Lys Lys Val Tyr  
 65 70 75 80

ctc tca gag tgc aag act ggg aat gga aag aac tac aga ggg acg atg	288
Leu Ser Glu Cys Lys Thr Gly Asn Gly Lys Asn Tyr Arg Gly Thr Met	
85 90 95	
tcc aaa aca aaa aat ggc atc acc tgt caa aaa tgg agt tcc act tct	336
Ser Lys Thr Lys Asn Gly Ile Thr Cys Gln Lys Trp Ser Ser Thr Ser	
100 105 110	
ccc cac aga cct aga ttc tca cct gct aca cac ccc tca gag gga ctg	384
Pro His Arg Pro Arg Phe Ser Pro Ala Thr His Pro Ser Glu Gly Leu	
115 120 125	
gag gag aac tac tgc agg aat cca gac aac gat ccg cag ggg ccc tgg	432
Glu Glu Asn Tyr Cys Arg Asn Pro Asp Asn Asp Pro Gln Gly Pro Trp	
130 135 140	
tgc tat act act gat cca gaa aag aga tat gac tac tgc gac att ctt	480
Cys Tyr Thr Thr Asp Pro Glu Lys Arg Tyr Asp Tyr Cys Asp Ile Leu	
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gag tgt gaa gag gaa tgt atg cat tgc agt gga gaa aac tat gac ggc	528
Glu Cys Glu Glu Glu Cys Met His Cys Ser Gly Glu Asn Tyr Asp Gly	
165 170 175	
aaa att tcc aag acc atg tct gga ctg gaa tgc cag gcc tgg gac tct	576
Lys Ile Ser Lys Thr Met Ser Gly Leu Glu Cys Gln Ala Trp Asp Ser	
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Gln Ser Pro His Ala His Gly Tyr Ile Pro Ser Lys Phe Pro Asn Lys	
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aac ctg aag aag aat tac tgt cgt aac ccc gat agg gag ctg cgg cct	672
Asn Leu Lys Lys Asn Tyr Cys Arg Asn Pro Asp Arg Glu Leu Arg Pro	
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225 230 235 240	
ccc cgc tgc aca aca cct cca cca tct tct ggt ccc acc tac cag tgt	768
Pro Arg Cys Thr Thr Pro Pro Pro Ser Ser Gly Pro Thr Tyr Gln Cys	
245 250 255	
ctg aag gga aca ggt gaa aac tat cgc ggg aat gtg gct gtt acc gtt	816
Leu Lys Gly Thr Gly Glu Asn Tyr Arg Gly Asn Val Ala Val Thr Val	
260 265 270	
tcc ggg cac acc tgt cag cac tgg agt gca cag acc cct cac aca cat	864
Ser Gly His Thr Cys Gln His Trp Ser Ala Gln Thr Pro His Thr His	
275 280 285	
aac agg aca cca gaa aac ttc ccc tgc aaa aat ttg gat gaa aac tac	912
Asn Arg Thr Pro Glu Asn Phe Pro Cys Lys Asn Leu Asp Glu Asn Tyr	
290 295 300	



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Ser Gln Val Arg Trp Glu Tyr Cys Lys Ile Pro Ser Cys Asp Ser Ser	
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Phe Thr Pro Glu Thr Asn Pro Arg Ala Gly Leu Glu Lys Asn Tyr Cys	
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Arg Asn Pro Asp Gly Asp Val Gly Gly Pro Trp Cys Tyr Thr Thr Asn	
515 520 525	

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Ser	Phe	Asp	Cys	Gly	Lys	Pro	Gln	Val	Glu	Pro	Lys	Lys	Cys	Pro	Gly	
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Arg	Val	Val	Gly	Gly	Cys	Val	Ala	His	Pro	His	Ser	Trp	Pro	Trp	Gln	
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Ile	Ser	Pro	Glu	Trp	Val	Leu	Thr	Ala	Ala	His	Cys	Leu	Glu	Lys	Ser	
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Pro	Arg	Pro	Ser	Ser	Tyr	Lys	Val	Ile	Leu	Gly	Ala	His	Gln	Glu	Val	
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Val	Ile	Thr	Asp	Lys	Val	Ile	Pro	Ala	Cys	Leu	Pro	Ser	Pro	Asn	Tyr	
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Val	Val	Ala	Asp	Arg	Thr	Glu	Cys	Phe	Ile	Thr	Gly	Trp	Gly	Glu	Thr	
		675					680					685				
caa	ggc	act	ttt	gga	gct	ggc	ctt	ctc	aag	gaa	gcc	cag	ctc	cct	gtg	2112
Gln	Gly	Thr	Phe	Gly	Ala	Gly	Leu	Leu	Lys	Glu	Ala	Gln	Leu	Pro	Val	
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Ile	Glu	Asn	Lys	Val	Cys	Asn	Arg	Tyr	Glu	Phe	Leu	Asn	Gly	Arg	Val	
	705				710					715					720	
caa	tcc	acc	gaa	ctc	tgt	gct	ggg	cat	ttg	gcc	gga	ggc	act	gac	agt	2208
Gln	Ser	Thr	Glu	Leu	Cys	Ala	Gly	His	Leu	Ala	Gly	Gly	Thr	Asp	Ser	
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tgc	cag	ggc	gac	agt	gga	ggc	cct	ctg	gtt	tgc	ttc	gag	aag	gac	aaa	2256
Cys	Gln	Gly	Asp	Ser	Gly	Gly	Pro	Leu	Val	Cys	Phe	Glu	Lys	Asp	Lys	
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Ser	Lys	Glu	Gln	Gln	Cys	Val	Ile	Met	Ala	Glu	Asn	Arg	Lys	Ser	Ser	
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Pro	His	Arg	Pro	Arg	Phe	Ser	Pro	Ala	Thr	His	Pro	Ser	Glu	Gly	Leu	
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Glu	Glu	Asn	Tyr	Cys	Arg	Asn	Pro	Asp	Asn	Asp	Pro	Gln	Gly	Pro	Trp	
	130					135					140					
Cys	Tyr	Thr	Thr	Asp	Pro	Glu	Lys	Arg	Tyr	Asp	Tyr	Cys	Asp	Ile	Leu	
145					150					155					160	
Glu	Cys	Glu	Glu	Glu	Cys	Met	His	Cys	Ser	Gly	Glu	Asn	Tyr	Asp	Gly	
				165					170					175		
Lys	Ile	Ser	Lys	Thr	Met	Ser	Gly	Leu	Glu	Cys	Gln	Ala	Trp	Asp	Ser	
			180					185					190			
Gln	Ser	Pro	His	Ala	His	Gly	Tyr	Ile	Pro	Ser	Lys	Phe	Pro	Asn	Lys	
		195					200					205				

Asn Leu Lys Lys Asn Tyr Cys Arg Asn Pro Asp Arg Glu Leu Arg Pro  
 210 215 220  
 Trp Cys Phe Thr Thr Asp Pro Asn Lys Arg Trp Glu Leu Cys Asp Ile  
 225 230 235 240  
 Pro Arg Cys Thr Thr Pro Pro Pro Ser Ser Gly Pro Thr Tyr Gln Cys  
 245 250 255  
 Leu Lys Gly Thr Gly Glu Asn Tyr Arg Gly Asn Val Ala Val Thr Val  
 260 265 270  
 Ser Gly His Thr Cys Gln His Trp Ser Ala Gln Thr Pro His Thr His  
 275 280 285  
 Asn Arg Thr Pro Glu Asn Phe Pro Cys Lys Asn Leu Asp Glu Asn Tyr  
 290 295 300  
 Cys Arg Asn Pro Asp Gly Lys Arg Ala Pro Trp Cys His Thr Thr Asn  
 305 310 315 320  
 Ser Gln Val Arg Trp Glu Tyr Cys Lys Ile Pro Ser Cys Asp Ser Ser  
 325 330 335  
 Pro Val Ser Thr Glu Gln Leu Ala Pro Thr Ala Pro Pro Glu Leu Thr  
 340 345 350  
 Pro Val Val Gln Asp Cys Tyr His Gly Asp Gly Gln Ser Tyr Arg Gly  
 355 360 365  
 Thr Ser Ser Thr Thr Thr Thr Gly Lys Lys Cys Gln Ser Trp Ser Ser  
 370 375 380  
 Met Thr Pro His Arg His Gln Lys Thr Pro Glu Asn Tyr Pro Asn Ala  
 385 390 395 400  
 Gly Leu Thr Met Asn Tyr Cys Arg Asn Pro Asp Ala Asp Lys Gly Pro  
 405 410 415  
 Trp Cys Phe Thr Thr Asp Pro Ser Val Arg Trp Glu Tyr Cys Asn Leu  
 420 425 430  
 Lys Lys Cys Ser Gly Thr Glu Ala Ser Val Val Ala Pro Pro Pro Val  
 435 440 445  
 Val Leu Leu Pro Asp Val Glu Thr Pro Ser Glu Glu Asp Cys Met Phe  
 450 455 460  
 Gly Asn Gly Lys Gly Tyr Arg Gly Lys Arg Ala Thr Thr Val Thr Gly  
 465 470 475 480  
 Thr Pro Cys Gln Asp Trp Ala Ala Gln Glu Pro His Arg His Ser Ile  
 485 490 495  
 Phe Thr Pro Glu Thr Asn Pro Arg Ala Gly Leu Glu Lys Asn Tyr Cys  
 500 505 510

Arg Asn Pro Asp Gly Asp Val Gly Gly Pro Trp Cys Tyr Thr Thr Asn  
 515 520 525  
 Pro Arg Lys Leu Tyr Asp Tyr Cys Asp Val Pro Gln Cys Ala Ala Pro  
 530 535 540  
 Ser Phe Asp Cys Gly Lys Pro Gln Val Glu Pro Lys Lys Cys Pro Gly  
 545 550 555 560  
 Arg Val Val Gly Gly Cys Val Ala His Pro His Ser Trp Pro Trp Gln  
 565 570 575  
 Val Ser Leu Arg Thr Arg Phe Gly Met His Phe Cys Gly Gly Thr Leu  
 580 585 590  
 Ile Ser Pro Glu Trp Val Leu Thr Ala Ala His Cys Leu Glu Lys Ser  
 595 600 605  
 Pro Arg Pro Ser Ser Tyr Lys Val Ile Leu Gly Ala His Gln Glu Val  
 610 615 620  
 Asn Leu Glu Pro His Val Gln Glu Ile Glu Val Ser Arg Leu Phe Leu  
 625 630 635 640  
 Glu Pro Thr Arg Lys Asp Ile Ala Leu Leu Lys Leu Ser Ser Pro Ala  
 645 650 655  
 Val Ile Thr Asp Lys Val Ile Pro Ala Cys Leu Pro Ser Pro Asn Tyr  
 660 665 670  
 Val Val Ala Asp Arg Thr Glu Cys Phe Ile Thr Gly Trp Gly Glu Thr  
 675 680 685  
 Gln Gly Thr Phe Gly Ala Gly Leu Leu Lys Glu Ala Gln Leu Pro Val  
 690 695 700  
 Ile Glu Asn Lys Val Cys Asn Arg Tyr Glu Phe Leu Asn Gly Arg Val  
 705 710 715 720  
 Gln Ser Thr Glu Leu Cys Ala Gly His Leu Ala Gly Gly Thr Asp Ser  
 725 730 735  
 Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Phe Glu Lys Asp Lys  
 740 745 750  
 Tyr Ile Leu Gln Gly Val Thr Ser Trp Gly Leu Gly Cys Ala Arg Pro  
 755 760 765  
 Asn Lys Pro Gly Val Tyr Val Arg Val Ser Arg Phe Val Thr Trp Ile  
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RGD containing peptide

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<210> 15  
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<223> Description of Artificial Sequence: Illustrative  
peptide

<400> 15

Leu Glu Lys Arg

1